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## OBSERVATIONS ON ABNORMAL COURSES OF INFECTION OF *PARAGONIMUS RINGERI*\*

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It is a well known fact that infection with *Paragonimus ringeri* is caused by the swallowing of the encysted larvae. It is, however, important to know whether these larvae, if freed from their cysts, can infect through the skin, mucous membrane or any wound on the skin of the host. It seems that this might be possible since they can penetrate the intestinal wall, diaphragm, connective tissues, muscles and some of the viscera of the host after the encysted larvae are swallowed. To test the possibility of such infections, we carried through experiments in an attempt to answer the following questions.

1. Can the freed larvae penetrate the sound skin of the host? The larvae after being freed from their cysts are injured in fresh water, and lose their power of movement, so that some other medium was necessary for the experiments. They are more active in artificial intestinal juice or in normal saline. To determine whether active larvae can penetrate the skin of the host under suitable conditions we experimented on mice, cats and new-born puppies. The results of these experiments are as follows:

(a) Although the freed larvae move actively in the artificial intestinal juice or normal saline, yet they can not penetrate the sound skin of the mice and puppies in a room temperature below 30° C., since their movement decrease below 37° C.

(b) We stretched three mice on a small plate after shaving off the hair of the abdominal wall and dropped upon them the artificial intestinal juice containing the freed larvae. We then put them into a warm chamber at 38° C. After one and a half hours we found that in one case there was a slight desquamation on the abdominal wall, but we could find no evidence of penetration by the larvae.

These experiments prove that the freed larvae cannot penetrate through the sound skin of the host.

2. Can the freed larvae infect through a wound in the body? It is conceivable that the freed larvae might penetrate a wound on the body. It is necessary, however, to try by experiment whether they can actually infect from an exposed wound of the host. On July 15, 1918, we dropped the normal saline with many freed larvae on fresh wounds, which we made in the backs of two dogs. After awhile we found

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several points of hemorrhages caused by the perforation of these larvae. Then we covered the wound with a watch glass and bound it to the body in order to prevent infection from the licking of the wound. One of the dogs died on August 20, thirty-five days after the experiment, and the other on September 10, having passed fifty-seven days after the experiment. By dissection, we could not find any distomes in the first dog, but in the last case two freed distomes were discovered in the chest cavity.

By these experiments we proved that occasionally the freed larvae can infect a host from a fresh wound on the body.

3. Can the freed larvae infect the host through the mouth? In Korea, R. Kawamura (*Tokyoer med. Woch. No.* 1986, 1916) proved experimentally that *Paragonimus ringeri* which is growing in its final host, can continue development after being fed to other animals. This mode of infection is very interesting in relation to lung distome disease, because many Koreans have the habit of eating the meat and the liver of dogs and other animals raw. If such animals had the young distomes wandering in their muscles, connective tissues and liver, this habit might lead to the infection of man. Therefore, we examined this point very carefully, using seven dogs, with these results:

(a) A new-born puppy was fed with 25 larvae, which were just freed from the cysts in the artificial intestinal juice, on July 31, 1917. It was killed on October 2, sixty-one days after feeding. On dissection, we found a wormcyst in the middle lobe of the left lung, in which were two distomes, and a freed distome in the left pleural cavity.

(b) A new-born puppy was fed with 25 larvae which had just been freed from their cysts, on Aug. 2, 1917. The puppy died on August 23, having passed twenty-one days after feeding. On dissection the next day, we found a distome in its right chest cavity, and numerous ankylostomes and ascarids which caused the death of the dog.

(c) A young dog was fed on Dec. 9, 1916, with 15 distomes which had lived for forty-two days in another dog, and killed on the twenty-fifth of the same month, fourteen days after feeding. On dissection we could not find any worms in the body.

(d) A young dog was fed on Aug. 19, 1918, with 20 distomes, which had lived for forty-two days in another dog. The dog died on the thirtieth day of that month, ten days after feeding. On dissection, we could not find any distomes in its body.

(e) A young dog was fed on July 8, 1918, with 27 distomes, which had lived for fourteen days in another dog, and 51 distomes on the thirty-first of the same month, which had lived for twenty days in another dog. Next day we killed this dog, five days having passed after the first and one day after the second feeding. On dissection, an hemorrhage was observed in the intestinal wall. This hemorrhage

probably was caused by the action of the distomes, therefore we looked for the worms with special care, but could not find any worms in the body.

(f) A young dog was fed on June 15, 1918, with 18 distomes, which had lived for eighteen days in another dog, and on the nineteenth of that month with 9 distomes which had lived for twenty-three days in another dog. On June 21 it was killed, having passed six and two days after first and second feeding. Careful dissection failed to disclose any worms.

(g) A young dog was fed on June 10, 1918, with 228 larvae just freed from their cysts and killed twenty hours after feeding. On dissection, some inflammation was observed here and there on the serous membrane of the viscera, and many hemorrhages were found in the intestinal wall. It is evident that these hemorrhages were caused by the perforation of the distomes, because we found 21 distomes in the abdominal cavity. The diaphragm and the lungs were intact. There were no distomes in the pleural cavity.

From these experiments we learned that the larvae which were just freed from the cysts as well as the encysted larvae can infect by way of the mouth, but that distomes which were in a more advanced stage of development in their host, cannot develop after feeding to other animals. This indicates that the worms, which are partly developed in one host, find it difficult to pierce the wall of the intestine when introduced into another host, because of the decrease in activity which comes with growth. We proved this fact by using the mucous membrane of lips and the conjunctiva of dogs. For example, if we put some newly freed larvae on the conjunctiva, or on the mucous membrane of the lips of a dog, they soon penetrate the mucous membrane, but the distomes, which are partly developed in one host, cannot bore through these membranes. While our experiments showed that partly grown larvae of *Paragonimus ringeri* could not be transferred from one host to another, two cases of such infection have been reported by Mr. R. Kawamura and by Dr. Ando\* (*Rept. Jap. Path. Soc.* v. 6, 1918). On account of these exceptional cases, it will be necessary to forbid the eating of the raw flesh and livers of animals which can harbor the lung fluke.

4. Can the freed larvae infect through mucous membranes outside the digestive tract? To ascertain the pathological changes in the orbits caused by *Paragonimus ringeri*, we dropped normal saline containing larvae just freed from their cysts, on the conjunctiva of dogs,

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\*Dr. Ando later repeated this experiment, using eighteen white rats. His results in this second experiment failed to show development in a second host of larvae which had lived for a period in one final host (*Tokyoer Med. Wochenschr.*, No. 2163, 1919).

cats and rabbits. In a little while, we found some small hemorrhages, which were caused by the penetration of the worms. In this experiment, nine rabbits, seven dogs and two monkeys were used, and were examined at various times after these experiments. Each animal showed the presence of the distomes after careful examination first of the orbits and then of the whole body. We proved that the distomes which entered into the orbits were to be found in that place for ten or fifteen days after the beginning of the experiments. But in the cases in which twenty days or more had passed after the experiment, they were found in the chest cavity and not in the orbits. It is very interesting to know how they found their way from the orbits to the chest cavity. We demonstrated this point on experimental animals, and will describe the two most interesting cases.

(a) On September 1, 1918, we put 14 distomes into the right, and 17 into the left orbit of a young dog by cutting open the capsule of Tenon. These distomes were collected from a dog, which was fed with a large number of the encysted larvae sixty-one days before. The dog died on the ninth of that month, eight days after the experiment. On dissection, there was found some muddy exudate in the pleural cavity. The lungs were congested a little and showed some irregular points of hemorrhages here and there, but we could not find any pathological changes, caused by penetration of the worms. We found a distome along the vena cava superior, near the lower end, of the trachea, and another distome on the diaphragm of the right side. In the dissection of the neck we found a distome, which was moving in the loose connective tissue of the right side, about the middle of the trachea, and another distome in the submucosa of the posterior wall of the pharynx. Both eyeballs were badly injured by the operation, but we could not find any worms in the eyeballs and in the orbits. We found only a small suppuration, which was due to the boring of the worms, and the subsequent infection by bacteria, in the tissue of the upper corner of the left orbit and in the left temporal muscle.

(b) On October 11, 1918, we put four distomes into the right and fourteen into the left eye of a big dog by the same operation. These distomes were all mature. The dog died on the twenty-fifth of that month, 14 days after the experiment. On dissection, 2 distomes were found; one of them was situated on the bifurcation of the internal maxillary artery and the superficial temporal artery, and the other worm was located in the masseter muscle around the masseter artery. The lungs and the other viscera were intact.

From these experiments we concluded that the distomes which were dropped on the conjunctiva, penetrate into the orbits and live there a certain number of days. Afterward they escape from the orbits and move to the chest cavity, wandering in the soft tissues.

Therefore, in the monkey's orbits, which are enclosed completely by the bones, they remained a very long time. In the case of a monkey, which was examined eighty-four days after the experiment, we found a living distome in the orbit instead of in the chest cavity.

#### SUMMARY

1. Young active larvae of *Paragonimus ringeri*, just freed from cysts, cannot penetrate the sound skin, but can enter through a fresh wound.
2. Such young distomes can infect the body by the mouth. Their course from the intestine to the lungs is very similar to the route taken by the encysted larvae.
3. Young distomes just freed from cysts can penetrate the mucous membrane outside of the digestive tract, like the conjunctiva, and bore through the tissues until they reach the lungs.
4. Our experiments indicate that other animals cannot be infected by distomes, which had started development in the final host.
5. Partly developed distomes cannot penetrate the mucous membrane, but, if transferred to the orbits of a suitable host, they penetrate the tissues and reach the lungs.